

PublisherInfo

PublisherName : Springer International Publishing
PublisherLocation : Cham
PublisherImprintName : Springer

I_xB, NF-_xB Regulation Model: Simulation Analysis of Small Number of Molecules

ArticleInfo

ArticleID : 64
ArticleDOI : 10.1155/2007/25250
ArticleCitationID : 25250
ArticleSequenceNumber : 7
ArticleCategory : Research Article
ArticleFirstPage : 1
ArticleLastPage : 4
ArticleHistory : RegistrationDate : 2007-3-21
Received : 2007-3-21
Revised : 2007-8-27
Accepted : 2007-11-8
OnlineDate : 2008-1-24
ArticleCopyright : Anamika Sarkar et al.2007
This article is published under license to BioMed Central Ltd. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
ArticleGrants :
ArticleContext : 136372007200711

Anamika Sarkar, [Aff1](#) [Aff2](#)

Corresponding Affiliation: [Aff1](#)

Email: sarkaranamika@gmail.com

Marina Meila, [Aff3](#)

Email: mmp@stat.washington.edu

Robert B Franza, [Aff1](#)

Email: bfranza@u.washington.edu

[Aff1](#) Bioengineering Department, Cell Systems Initiative, University of Washington, Seattle, WA 98195, USA

[Aff2](#) Department of Pharmacology and Systems Therapeutics, Mount Sinai School of Medicine, P.O. Box 1215, One Gustave L. Levy Place, New York, NY 10029, USA

[Aff3](#) Statistics Department, University of Washington, Seattle, WA 98195, USA

Abstract

The regulation of I κ B, NF- κ B is of foremost interest in biology as the transcription factor NF- κ B has multiple target genes. We have modeled a previously published model by Hoffmann et al. (2002) of I κ B, NF- κ B mathematically as discrete reaction systems. We have used stochastic algorithm to compare the results when there are large and small numbers of molecules available in a finite volume for each protein. Our results for small number of molecules show that with continuous presence of stimulation, nuclear NF- κ B oscillates continuously in every individual cell rather than damping, which was observed in cell population results. This characteristic of the system is missed when averaged behavior is studied.

Publisher note

To access the full article, please see PDF.

References

1. Ghosh S, May MJ, Kopp EB: **NF- κ B and rel proteins: evolutionary conserved mediators of immune responses.** *Annual Review of Immunology* 1998, **16**: 225-260. [10.1146/annurev.immunol.16.1.225](#)
2. Gonzalez-Crespo S, Levine M: **Related target enhancers for dorsal and NF- κ B signaling pathways.** *Science* 1994, **264**(5156):255-258. [10.1126/science.8146656](#)
3. Malek S, Huxford T, Ghosh G: **I κ B α functions through direct contacts with the nuclear localization signals and the DNA binding sequences of NF- κ B.** *Journal of Biological Chemistry* 1998, **273**(39):25427-25435. [10.1074/jbc.273.39.25427](#)
4. Hoffmann A, Levchenko A, Scott ML, Baltimore D: **The I κ B-NF- κ B signaling module: temporal control and selective gene activation.** *Science* 2002, **298**(5596):1241-1245. [10.1126/science.1071914](#)
5. Nelson DE, Ihewaba AEC, Elliott M, et al.: **Oscillations in NF- κ B signaling control the dynamics of gene expression.** *Science* 2004, **306**(5696):704-708. [10.1126/science.1099962](#)

6. Barken D, Wang CJ, Kearns J, Cheong R, Hoffmann A, Levchenko A: **Comment on oscillations in NF- κ B signaling control the dynamics of the gene expression.** *Science* 2005,**308**(5718):52. 10.1126/science.1107904
7. Nelson DE, Horton CA, See V, *et al.*: **Response to comment on oscillations in NF- κ B signaling control the dynamics of the gene expression.** *Science* 2005,**308**(5718):52. 10.1126/science.1107904
8. Lauffenburger DA: *Receptors: Models for Binding, Trafficking and Signaling.* Oxford University Press, Oxford, UK; 1993.
9. Bhalla US, Iyengar R: **Emergent properties of networks of biological signaling pathways.** *Science* 1999,**283**(5400):381-387. 10.1126/science.283.5400.381
10. Kholodenko BN: **Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades.** *European Journal of Biochemistry* 2000,**267**(6):1583-1588.
11. Bentele M, Lavrik I, Ulrich M, *et al.*: **Mathematical modeling reveals threshold mechanism in CD95-induced apoptosis.** *Journal of Cell Biology* 2004,**166**(6):839-851. 10.1083/jcb.200404158
12. [<http://physiome.org>]
13. [<http://www.nrcam.uchc.edu/login/login.html>]
14. Luby-Phelps K, Weisiger RA: **Role of cytoarchitecture in cytoplasmic transport.** *Comparative Biochemistry and Physiology B* 1996,**115**(3):295-306. 10.1016/S0305-0491(96)00176-9
15. Goodsell DS: **Inside a living cell.** *Trends in Biochemical Sciences* 1991,**16**(6):203-206.
16. Berg OG: **The influence of macromolecular crowding on thermodynamic activity: solubility and dimerization constants for spherical and dumbbell-shaped molecules in a hard-sphere mixture.** *Biopolymers* 1990,**30**(11-12):1027-1037. 10.1002/bip.360301104
17. Han J, Herzfeld J: **Macromolecular diffusion in crowded solutions.** *Biophysical Journal* 1993,**65**(3):1155-1161. 10.1016/S0006-3495(93)81145-7
18. Lahav G, Rosenfeld N, Sigal A, *et al.*: **Dynamics of the p53-Mdm2 feedback loop in individual cells.** *Nature Genetics* 2004,**36**(2):147-150. 10.1038/ng1293
19. Vilar JMG, Kueh HY, Barkai N, Leibler S: **Mechanisms of noise-resistance in genetic oscillators.** *Proceedings of the National Academy of Sciences of the United States of America* 2002,**99**(9):5988-5992. 10.1073/pnas.092133899
20. Sachs K, Perez O, Pe'er D, Lauffenburger DA, Nolan GP: **Causal protein-signaling networks derived from multiparameter single-cell data.** *Science* 2005,**308**(5721):523-529. 10.1126/science.1105809
21. McAdams HH, Arkin A: **Stochastic mechanisms in gene expression.** *Proceedings of the National Academy of Sciences of the United States of America* 1997,**94**(3):814-819. 10.1073/pnas.94.3.814
22. McAdams H, Arkin H: **It's noisy business! Genetic regulation at the nanomolecular scale.** *Trends Genetics* 1999,**15**(2):65-69. 10.1016/S0168-9525(98)01659-X
23. Gonze D, Halloy J, Goldbeter A: **Robustness of circadian rhythms with respect to molecular noise.** *Proceedings of the National Academy of Sciences of the United States of America* 2002,**99**(2):673-678. 10.1073/pnas.022628299

24. Srivastava R, You L, Summers J, Yin J: **Stochastic vs deterministic modeling of intracellular viral kinetics.** *Journal of Theoretical Biology* 2002,**218**(3):309-321. 10.1006/jtbi.2002.3078
25. Bhalla US: **Signaling in small subcellular volumes. I. Stochastic and diffusion effects on individual pathways.** *Biophysical Journal* 2004,**87**(2):733-744. 10.1529/biophysj.104.040469
26. Bhalla US: **Signaling in small subcellular volumes. II. Stochastic and diffusion effects on synaptic network properties.** *Biophysical Journal* 2004,**87**(2):745-753. 10.1529/biophysj.104.040501
27. [<http://www.cellsystems.org/teams/modeling/projects/sigtran/index.html>]
28. Morton-Firth CJ, Bray D: **Predicting temporal fluctuations in an intracellular signalling pathway.** *Journal of Theoretical Biology* 1998,**192**(1):117-128. 10.1006/jtbi.1997.0651
29. Gillespie DT: **A general method for numerically simulating the stochastic time evolution of coupled chemical reactions.** *Journal of Computational Physics* 1976,**22**(4):403-434. 10.1016/0021-9991(76)90041-3
30. Gibson MA, Bruck J: **Efficient exact stochastic simulation of chemical systems with many species and many channels.** *Journal of Physical Chemistry A* 2000,**104**(9):1876-1889. 10.1021/jp993732q
31. Gillespie DT: **Exact stochastic simulation of coupled chemical reactions.** *Journal of Physical Chemistry* 1977,**81**(25):2340-2361. 10.1021/j100540a008
32. Elliott DF: *Handbook of Digital Signal Processing: Engineering Applications.* Academic Press, New York, NY, USA; 1987.
33. Grenander U, Szego G: *Toeplitz Forms and Their Applications.* Chelsea, New York, NY, USA; 1984.
34. [<http://www.mathworks.com>]
35. Perkins ND, Gilmore TD: **Good cop, badcop: the different faces of NF- κ B.** *Cell Death and Differentiation* 2006, **13**: 759-772. 10.1038/sj.cdd.4401838
36. **Aberrant rel/nfkb genes and activity in human cancer.** *Oncogene* 1999,**18**(49):6938-6947. 10.1038/sj.onc.1203221